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FOX, DAVID T	

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ANTHONY J. KINNEY, EDGAR BENJAMIN CAHOON,
HOWARD GLENN DAMUDE and ZHAN-BIN LIU

Appeal 2009-015186
Application 10/776,311
Technology Center 1600

Before ERIC GRIMES, MICHAEL P. COLAIANNI, and
BEVERLY A. FRANKLIN, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This is an appeal under 35 U.S.C. § 134 involving claims to a transgenic oilseed plant. The Examiner has rejected the claims as

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

The Specification discloses that "[t]here are two main families of polyunsaturated fatty acids (PUFAs), specifically, the omega-3 fatty acids and the omega-6 fatty acids" (Spec. 1: 29-30). The Specification discloses that "[r]esearch has shown that omega-3 fatty acids reduce the risk of heart disease as well as having a positive effect on children's development" (*id.* at 2: 15-16).

Claims 1, 12, 16 and 26 are on appeal. The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Claims 1 and 12 are representative and read as follows:

1. A transgenic oilseed plant that produces mature seeds in which the total seed fatty acid profile comprises at least 1.0% of at least one omega-3 polyunsaturated fatty acid having at least twenty carbon atoms and five or more carbon-carbon double bonds wherein said transgenic oilseed plant comprises in its genome at least two transgenic nucleic acid sequences encoding at least two different polypeptides and further wherein at least one polypeptide has desaturase activity and at least one polypeptide has elongase activity.

12. The oilseed plant of Claim 1 wherein the polyunsaturated fatty acid is an omega-3 fatty acid selected from the group consisting of eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA).

Issue

The Examiner has rejected claims 1, 12, 16 and 26 under 35 U.S.C. § 103(a) as being obvious in view of Knutzon,[2] Abbott Laboratories,[3] and either Mukerji[4] or Browse.[5]

The Examiner finds that Knutzon suggests "plant transformation with a combination of desaturase and elongase transgenes for the production in plants of PUFAs [polyunsaturated fatty acids] with at least 20 carbons and at least 5 carbon-carbon double bonds" (Answer 5). The Examiner finds that Abbott Laboratories "teaches the isolation of elongase genes necessary for the production of polyunsaturated 20-carbon fatty acids in plants," and suggests transforming plants with an elongase gene under the control of a seed-specific promoter to produce PUFAs in seed oils (*id.* at 6). The Examiner finds that Browse and Mukerji both disclose a gene encoding an omega-3 desaturase (a.k.a. delta 17 desaturase) enzyme, which converts arachidonic acid to eicosapentaenoic acid (*id.* at 7).

The Examiner concludes that it would have been obvious to one of ordinary skill in the art to modify Knutzon's method "by incorporating the elongase genes taught by ABBOTT LABORATORIES under the control of a seed-specific promoter; given the suggestion to do so by Knutzon et al and ABBOTT LABORATORIES" (*id.* at 7-8), and also to "modify that method by incorporating the omega 3/delta 17 desaturase gene … for the production of EPA in the oil of the transgenic Brassica seeds" (*id.* at 8). The Examiner

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[2] Knutzon et al., US 6,075,183, issued June 13, 2000
[3] Abbott Laboratories, WO 02/08401 A2, published Jan. 31, 2002
[4] Mukerji et al., US 7,211,656 B2, issued May 1, 2007
[5] Browse et al., US 6,884,921 B2, issued Apr. 26, 2005

reasons that "[g]iven the high levels of novel PUFA produced by the transgenic organisms ... of Knutzon ... one of ordinary skill in the art would have reasonably expected the instantly claimed levels of EPA in the seed oil; as influenced by the highly expressed seed-specific napin promoter and the high proportion of oil in Brassica seeds" (*id.*).

Appellants contend that the cited references do not provide a reasonable expectation of success because "the individual enzymatic conversions efficiencies in plants, disclosed in each of the references, are not sufficient to enable an accumulation in seed oil of at least 1% DHA or EPA" (Appeal Br. 10).

The issue presented is: Does the evidence of record support the Examiner's conclusion that the cited references provide a reasonable expectation of obtaining a transgenic oilseed plant that produces seeds in which the fatty acids include at least 1.0% of omega-3 polyunsaturated fatty acid(s) having at least twenty carbon atoms and five or more carbon-carbon double bonds?

Findings of Fact

1. Plants naturally produce fatty acids including linoleic acid (18 carbon atoms, 2 double bonds) and α-linolenic acid (18 carbon atoms, 3 double bonds) (Knutzon, Fig. 1).

2. Eicosapentaenoic acid (EPA) can be made from α-linolenic acid by a series of three chemical reactions catalyzed by the enzymes delta-6 desaturase (Δ6), elongase (elo), and delta-5 desaturase (Δ5) (Abbott Laboratories, Fig. 1).

3. EPA is an omega-3 (ω3) polyunsaturated fatty acid with at least twenty carbon atoms and at least five carbon-carbon double bonds (*see* claim 12).

4. Knutzon discloses that "major long chain PUFAs of importance include docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), which are primarily found in different types of fish oil" (Knutzon, col. 1, ll. 24-27).

5. Knutzon discloses that "[n]ucleic acid sequences and constructs encoding fatty acid desaturases, including Δ5-desaturases, Δ6-desaturases, and Δ12-desaturases, are used to generate transgenic plants.... Expression of the desaturases ... in the plant system permit[s] the large scale production of poly-unsaturated long chain fatty acids such as docosahexaenoic acid, eicosapentaenoic acid," etc. (*id.*, abstract).

6. Knutzon discloses that "seed oil components can be manipulated through expression of desaturase genes, either alone or in combination with other genes such as elongases, to provide seed oils having a particular PUFA profile in concentrated form" (*id.* at col. 5, ll. 4-7).

7. Knutzon discloses isolation of DNA encoding Δ5-desaturase and Δ6-desaturase enzymes (*id.* at col. 13, l. 61 to col. 15, l. 55).

8. Knutzon discloses transgenic *Brassica napus* plants containing plasmid pCGN5538, which includes a Δ6 desaturase gene under the control of the napin seed specific promoter (*id.* at col. 23, l. 19-col. 24, l. 9).

9. Knutzon discloses that analysis of seeds from six different plants transformed with a Δ6 desaturase gene showed that all but one of the plants produced seeds containing GLA (γ-linolenic acid) (*id.* at col. 24, ll. 10-15).

10. Δ6 desaturase converts linoleic acid to γ-linolenic acid (*id.*, Fig. 1).

11. Knutzon discloses that control seeds (LP004; Knutzon, col. 24, l. 13) contained no more than 0.01% GLA (Table 5, column headed "18:3ga"), while the seeds of the transgenic plants contained up to 15.67% GLA (*id.* at Table 5, seed 5538-4-8).

12. Knutzon discloses transgenic *Brassica napus* plants containing a Δ5 desaturase gene under the control of the napin seed specific promoter (*id.* at col. 19, l. 30 to col. 22, l. 51, Table 5).

13. Knutzon discloses that seeds from transformed plants showed two fatty acids not present in control plants, which were tentatively identified as "the expected products of Δ5 desaturation of oleic and linoleic acids" (*id.* at col. 22, ll. 44-51).

14. Knutzon concludes that the "results show that desaturases with three different substrate specificities can be expressed in a heterologous system and used to produce poly-unsaturated long chain fatty acids" (*id.* at col. 24, ll. 20-23).

15. Abbott Laboratories discloses a DNA sequence which encodes "a functionally active elongase which utilizes a polyunsaturated fatty acid or a monounsaturated fatty acid as a substrate" (Abbott 5:10-21; 35: 1-2).

16. Abbott Laboratories discloses that "until the present invention, no elongase had been identified which was active on substrate fatty acids in the pathways for the production of long chain PUFAs and, in particular … eicosapentaenoic acid (EPA)" (*id.* at 4:17-30).

17. Abbott Laboratories discloses transgenic plants containing vectors encoding the elongase DNA sequence, "wherein expression of the nucleotide sequence of the vector results in production of a polyunsaturated fatty acid in seeds of the transgenic plant" (*id.* at 7: 1-14).

18. Abbott Laboratories discloses introducing the isolated elongase-encoding DNA into a host cell to convert a substrate PUFA into a product PUFA (*id.* at 7: 24 to 8:2) and exposing the product PUFA to a desaturase to produce, e.g., EPA (*id.* at 8: 8-15).

19. Browse discloses "an ω-3 fatty acyl desaturase gene" (Browse, col. 3, ll. 21-22).

20. Browse discloses that transgenic plants transformed with the ω-3 fatty acyl desaturase gene were sprayed with arachidonic acid (a.k.a. Δ5,8,11,14–20:4), an ω-6 fatty acid (*id.* at col. 19, ll. 3-8, 34-35).

21. Browse discloses that the transgenic plants converted the exogenously applied ω-6 fatty acids into ω-3 fatty acids, including EPA (a.k.a., Δ5,8,11,14,17–20:5; *id.* at col. 18, ll. 58-61) (*id.* at col. 20, ll. 14-18).

22. Browse discloses that expression of the ω-3 fatty acyl desaturase produces

> transgenic plants that are capable of efficiently converting ω-6 fatty acids, including fatty acids having a carbon chain of greater than 18 carbons ... to the corresponding ω-3 fatty acids, thus producing plant cells and lipids obtained therefrom that have an altered fatty acid profile. Such plants include plants that are commonly grown for oil production, including, but not limited to, rapeseed, corn, canola, safflower, soybean, sunflower, peanut, etc.

(Browse, col. 12, ll. 16-26.)

23. Browse discloses that "[s]eed-specific promoters are preferred" (*id.* at col. 12, ll. 48-49).

24. Robert[6] discloses that

> Abbadi et al. (2004) transferred a Δ6 desaturase and a Δ5 desaturase ... as well as a Δ6 elongase ... into flax ... in order to produce EPA.... They were able to produce low but significant levels of AA [arachidonic acid] (1.5%) and EPA (1.0%) (Table 1) in the seed, presumably by the action of the introduced genes on the precursor fatty acids LA and ALA, respectively.

(Robert, 105.)

Principles of Law

"Obviousness does not require absolute predictability of success... For obviousness under § 103, all that is required is a reasonable expectation of success." *In re O'Farrell*, 853 F.2d 894, 903-04 (Fed. Cir. 1988).

Analysis

Claim 1 is directed to a transgenic oilseed plant, expressing an exogenous desaturase and an exogenous elongase, that produces mature seeds in which the fatty acids include at least 1.0% of an omega-3 polyunsaturated fatty acid having at least twenty carbon atoms and at least five carbon-carbon double bonds.

Knutzon discloses transgenic plants containing DNA encoding the Δ5 and Δ6 desaturase enzymes involved in the EPA synthesis pathway (FFs 7-13). Knutzon suggests the transformation of seed oil plants with the

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[6] Robert et al., *Production of Eicosapentaenoic and Docosahexaenoic Acid-Containing Oils in Transgenic Land Plants for Human and Aquaculture Nutrition*, 8 Marine Biotechnology 103-109 (2006).

desaturase genes, and other genes such as elongase, in order to modify the fatty acid profile of the seed oil (FF 6). Abbott Laboratories discloses isolated DNA encoding an elongase involved in the synthesis of long-chain fatty acids (FFs 15, 16). It would have been obvious to combine the elongase-encoding DNA with Knutzon's Δ5 and Δ6 desaturase genes in a seed oil plant because Knutzon expressly suggests doing so in order to permit large-scale production of EPA (FF 5).

Browse discloses isolated DNA that encodes a ω-3 desaturase (a.k.a. Δ17 desaturase), which converts the ω-6 fatty acid arachidonic acid into EPA (FF 19-21). In view of Browse's disclosure, it would have been obvious to one of ordinary skill in the art to modify the seed oil plant suggested by Knutzon and Abbott Laboratories to contain Browse's ω-3 desaturase in order to increase the amount of EPA in the seeds, because Browse discloses that transgenic plants expressing the ω-3 desaturase can efficiently convert ω-6 fatty acids into ω-3 fatty acids (FF 22) and Knutzon discloses that EPA is one of the "major long chain PUFAs of importance" (FF 4).

Appellants argue that the "cited references do not demonstrate accumulation in seed oil of an oilseed plant of at least 1% DHA or EPA. Further, when taken together the individual enzymatic conversions efficiencies in plants, disclosed in each of the references, are not sufficient to enable an accumulation in seed oil of at least 1% DHA or EPA" (Appeal Br. 10).

This argument is not persuasive. Knutzon and Browse disclose that the Δ5, Δ6, and ω-3 desaturase genes were expressed in transgenic plants

(FFs 14, 21), and Abbott Laboratories discloses that expression of its elongase gene in transgenic plants results in producing PUFAs in the seeds (FF 17). Knutzon discloses that plants expressing the Δ6 desaturase, for example, produced seeds having γ-linolenic acid (produced by Δ6 desaturase acting on linoleic acid) in amounts up to 15.67% of total fatty acids. Since the references disclose that all of the desaturase and elongase genes are expressed in transgenic plants, and Knutzon shows that the Δ6 desaturase activity can produce well over 1% of a desired fatty acid, those of skill in the art would have reasonably expected that the transgenic plants made obvious by the cited references would produce seeds having at least 1% EPA among the fatty acids in their oil. Obviousness does not require an absolute expectation of success, but only a reasonable expectation of success.

Appellants cite Robert as evidence that "[f]atty acids are desaturated while part of membrane lipids, they are elongated while attached to acyl-CoA. Thus, fatty acids need to pass in and out of the phospholipids in the plant cell membrane as part of the pathway to synthesizing EPA. This step was thought to be a major block in converting ALA [α-linolenic acid] to EPA in plants." (Appeal Br. 10).

This argument is also not persuasive. Robert summarizes previous work by Abbadi, and states that Abbadi was "able to produce low but significant levels of AA (1.5%) and EPA (1.0%) … in the seed" (FF 24). Although Robert later refers to "the problems with acyl shuttling between PC and CoA pools observed by Abbadi" (Robert 105, right col.), Appellants have pointed to nothing in Robert that would lead a skilled worker to expect that co-expression of elongase and Δ5, Δ6, and ω-3 desaturase genes would

not achieve the claimed 1% level of EPA. In fact, Abbadi supports the opposite conclusion, since it discloses production of 1% EPA in seeds of plants expressing desaturase and elongase genes, even with the "problems" referred to by Robert. In addition, the transgenic plants made obvious by Knutzon, Abbott Laboratories, and Browse include an ω-3 desaturase gene, which would be expected to convert arachidonic acid to EPA, and thereby increase the production of EPA compared to the Abbadi system described by Robert.

Conclusion of Law

The evidence of record supports the Examiner's conclusion that the cited references provide a reasonable expectation of obtaining a transgenic oilseed plant that produces seeds in which the fatty acids comprise at least 1.0% of omega -3 polyunsaturated fatty acid(s) having at least twenty carbon atoms and five or more carbon-carbon double bonds.

SUMMARY

We affirm the rejection of claims 1, 12, 16 and 26 under 35 U.S.C. § 103(a).

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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